## Interactions of health, disease, and nutrition in dairy calves

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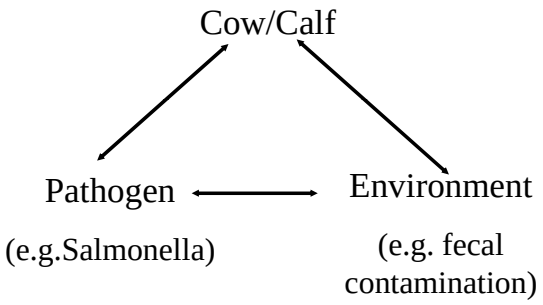
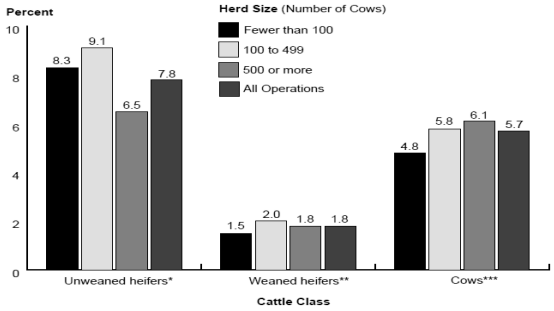



## How are we doing with calves?

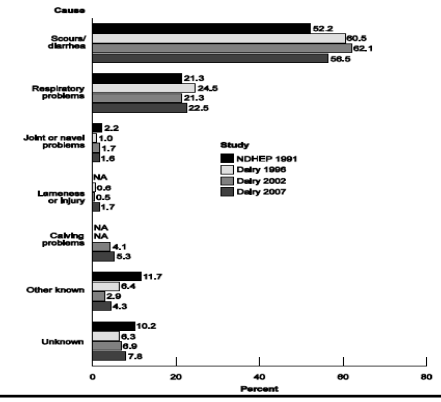
**Percentage of Unweaned Heifers, Weaned Heifers, and Cows that Died During 2006, by Herd Size**




*As a percentage of heifers born during 2006 and alive at 48 hours.
**As a percentage of January 1, 2007, heifer inventory (weaning age to calving).
***As a percentage of January 1, 2007, cow inventory.

NAHMS, 2007

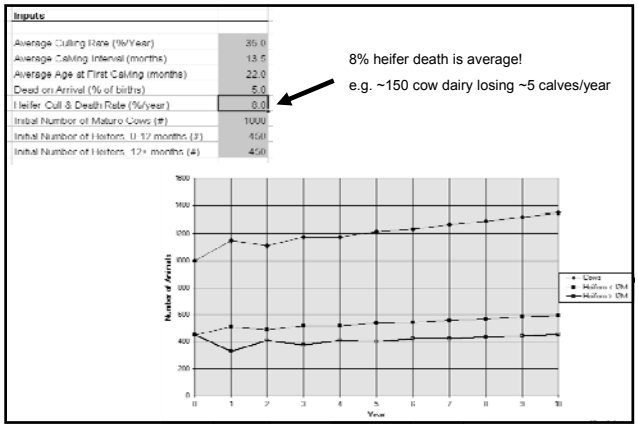
**Percentage of Unweaned Heifer Deaths by Cause**




## Not so good!
## Why bother with good youngstock programs?

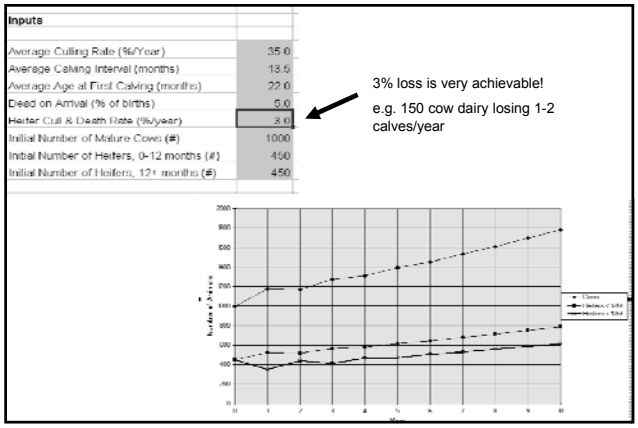
- Herd Growth if you want
- Animals to sell if you want
- Better culling decisions
- More milk

- We like calves




8% heifer death is average!

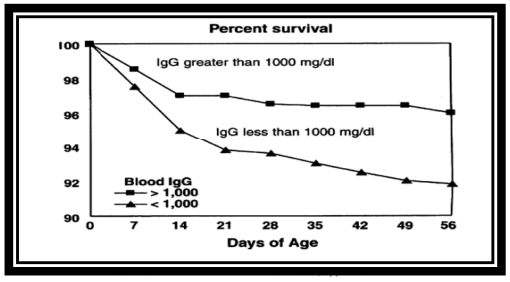
e.g. ~150 cow dairy losing ~5 calves/year




3% loss is very achievable!

e.g. 150 cow dairy losing 1-2 calves/year

## Live Calves




**PASSIVE TRANSFER!!**

## Colostrum *vs.* Milk

Table 1
Composition of colostrum, transition milk and whole milk of Holstein cows

| | Colostrum | Transition milk (milking postpartum) | | Milk |
|---|---|---|---|---|
| Parameter | 1 | 2 | 3 | 6 |
| Specific gravity | 1.056 | 1.040 | 1.035 | 1.032 |
| Total solids (%) | 23.9 | 17.9 | 14.1 | 12.9 |
| Fat (%) | 6.7 | 5.4 | 3.9 | 4.0 |
| Total protein (%) | 14.0 | 8.4 | 5.1 | 3.1 |
| Casein (%) | 4.8 | 4.3 | 3.8 | 2.5 |
| Albumin (%) | 6.0 | 4.2 | 2.4 | 0.5 |
| Immunoglobulins (%) | 6.0 | 4.2 | 2.4 | 0.09 |
| IgG (g/100 mL) | 3.2 | 2.5 | 1.5 | 0.06 |
| Lactose (%) | 2.7 | 3.9 | 4.4 | 5.0 |
| IGF-I (µg/L) | 341 | 242 | 144 | 15 |
| Insulin (µg/L) | 65.9 | 34.8 | 15.8 | 1.1 |
| Ash (%) | 1.11 | 0.95 | 0.87 | 0.74 |
| Calcium (%) | 0.26 | 0.15 | 0.15 | 0.13 |
| Magnesium (%)[ | 0.04 | 0.01 | 0.01 | 0.01 |
| Zinc (mg/100 mL) | 1.22 | — | 0.62 | 0.3 |
| Manganese (mg/100 mL) | 0.02 | — | 0.01 | 0.004 |
| Iron (mg/100 g) | 0.20 | | | 0.05 |
| Cobalt (µg/100 g) | 0.5 | — | — | 0.10 |
| Vitamin A (µg/100 mL) | 795 | 190 | 113 | 34 |
| Vitamin E (µg/g fat) | 84 | 76 | 36 | 13 |
| Riboflavin (µg/mL) | 4.83 | 2.71 | 1.85 | 1.47 |
| Vitamin $B_{12}$ (µg/100 mL) | 4.9 | — | 2.5 | 0.6 |
| Folic acid (µg/100 mL) | 0.8 | | 0.2 | 0.2 |
| Choline (mg/mL) | 0.7 | 0.34 | 0.23 | 0.13 |

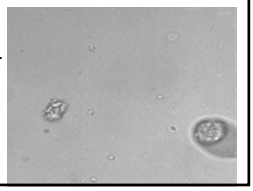
Godden S. Vet Clin North Am Food Anim Pract. 2008 Mar;24(1):19-39.

## Monitoring Passive Transfer

- Serum total proteins
  - TP estimates IgG levels
- Frequency
  - Dependent on herd size & calving rate
  - 1x/month < 1,000 cows
  - 2x/month > 1,000 cows
- Red top tubes
  - Clot and spin
  - Sit for 24 hours
- Refractometer
  - $250
- Group of 12 healthy calves
  - 24 hrs - 7 days of age
  - Goal: TP ≥ 5.2mg/dl in > 9/12 calves

## Agents associated with Calf Scours

- Bacteria
  - *E. coli, Salmonella, Clostridium, Sarcina, etc.*
- Viruses
  - Rotavirus, Coronavirus, BVD*, etc.*
- Protozoa
  - ***Cryptosporidium****, Giardia, etc.*



## Cattle agents that are zoonotic in North America

- Bacteria
  - *E. coli, Salmonella, Listeria, etc.*
- Viruses
  - *None? (Rabies)*
- Protozoa
  - ***Cryptosporidium**, Giardia, etc.*

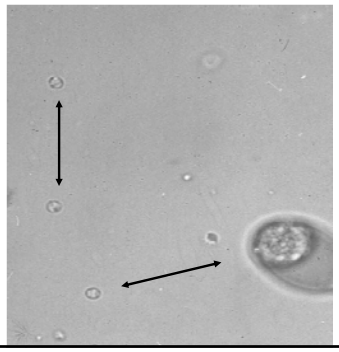
## *Cryptosporidium*

The pathogen most commonly diagnosed in association with calf scours

## Crypto Background Information

- Pathogenic Protozoa of Phylum Apicomplexa
- Worldwide Distribution
- Monoxenous life cycle
- Sporulated oocyst
- 4-5 micro meters

## *Cryptosporidium parvum*



## Prevalence

- USA
  - Garber, 1994
- BC
  - Olson, 1997
- Quebec
  - Ruest, 1998
- Ontario
  - Trotz-Williams
- Argentina
  - Del Coco, 2008

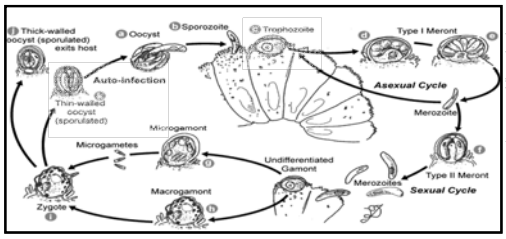
60-95% Herds

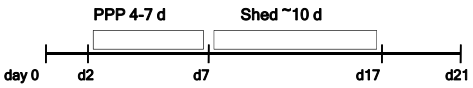
20-80% Calves

Up to 80% within herd prevalence

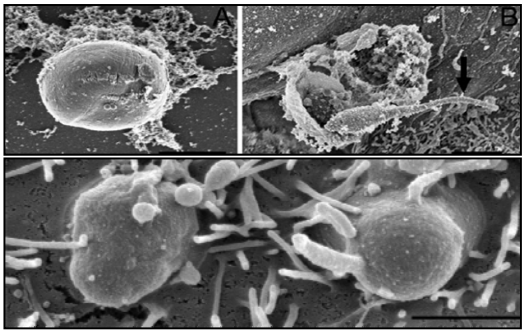
- Switzerland
  - Uhde, 2008
- Norway
  - Gulliksen, 2009
- Sweden
  - Silverlås, 2009
- Netherlands
  - Bartels, 2010
- Belgium
  - De Graaf, 1999

## Mechanism of disease



## Mechanism of disease




H. Borowski et al. Parasitology. 2010. 137. 13–26.

## Background Information

- Survivability
  - Fecal material: 100 – 400 d
  - Soil: >160 d
  - Water: >160 d
  - A portion remain viable after freezing

## Background Information

- Disinfection
  - Resistant to:
    - bleach
    - Virkon
    - iodophores
    - 10% formalin works though?
  - Effective:
    - Pasteurization
    - Steam disinfection

## Transmission:

Mostly fecal oral, but…

Mouth Parts

And rodents?

## Quantify risk calves pose:

- Study Design:
  - 478 dairy calves recruited from a longitudinal study
  - 4-21 days old
  - 37 farms in New York
  - Oocysts enumerated by sugar flotation and microscopy

**Number of *Cryptosporidium parvum* oocysts or *Giardia* spp cysts shed by dairy calves after natural infection**

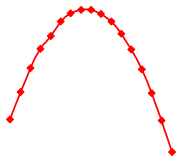
Daryl V. Nydam, DVM; Susan E. Wade, PhD; Stephanie L. Schaaf, BA; Hussni O. Mohammed, BVSc, MPVM, PhD

## Quantify risk calves pose

- Computation:

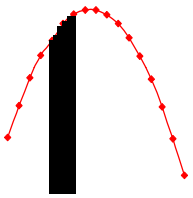
$\int_a^b [ (32105.2 \text{ age}) - (1398.6 \text{ age}^2) ] \, dx$

a=age at onset
b=age at termination



## Quantify risk calves pose

- Example:
  - Calf sheds from 8 to 10 days old
  - Model predicts 350,388 oocysts/g
  - Data=5.4kg/day



## Quantify risk calves pose

- Conclusion:
  - 189,095,200 oocysts shed by average infected calf
  - This is a significant number of oocysts with potential for environmental contamination and transmission to susceptible hosts
  - $ID_{50}$ =132 oocysts for seronegative people
  - Calves infected with as few as 50 oocysts
  - Consistently create scours with 6000 oocysts

## Do people get Crypto from cows?

- Short Answer: YES
- Long Answer: SOMETIMES
- Need to talk about nomenclature and genotyping

## *Cryptosporidium* species / genotypes

- *C. parvum*
  - Genotype H (1); C (2)
    - C. hominus; C. parvum
- *C. hominis*
- *C. andersoni (muris)*
- *C. muris*
- *C. felis*
- *C. serpentis*
- *C. etc*.

## Species / Genotyping

Cattle often implicated as source of *C. parvum* oocysts in drinking-water outbreaks

At least 2 species that infect humans

- *C. hominis*
- *C. parvum*

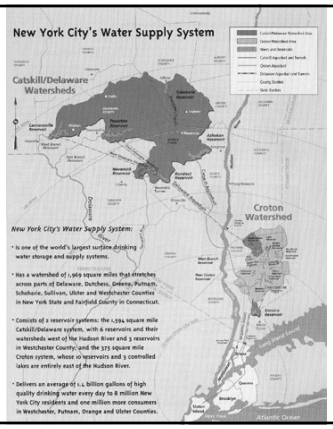
## Objective

Determine the potential risk of *Cryptosporidium parvum* and C. hominis in dairy herds in the NYC Watershed

## Risk of infection with *Cryptosporidium parvum* and *Cryptosporidium hominis* in dairy cattle in the New York City watershed

Daryl V. Nydam, DVM, PhD; Gabbriella Lindergard, PhD; Fiametta Santucci, PhD; Stephanie L. Schaaf, BA; Susan E. Wade, PhD; Hussni O. Mohammed, BVSc, MPVM, PhD

AJVR, Vol 66, No. 3, March 2005 



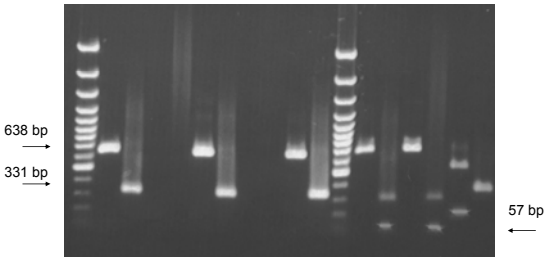
## Materials and Methods

Study Design:

- Target Population: Dairies in 5 counties in NYCW
- 27 randomly selected farms; weighted proportional sampling of calves at risk
- Human fecal samples from outbreaks and sporadic cases
- *C. parvum* oocysts detected by quantitative concentration flotation

## Public Health Concerns and Genotyping

437 isolates, 95% Confidence




## Conclusions

Cattle in the NYCW have only the *C. parvum* genotype

Cattle may **not** be the 1° source of human drinking water outbreaks

## Discussion

Review of North American drinking water outbreaks; all but 1 associated with H genotype *(C. hominus)*

Cattle are not the likely source of waterborne outbreaks which are of the H genotype *(C. hominus)*
at least in North America

In Europe waterborne outbreaks have been associated with C. parvum type 2 / C. hominus ??

## Treatment/Prophylaxis

- Allicin
- Trimethoprim-sulfa, sulfadimidine, sulfadimethoxine
- Amprolium
- Ionophores?
  - Effective dose ~ $LD_{50}$

## Treatment/ Prophylaxis

- Azithromycin
  - ~$20/g
  - 1g/day for 7 days → $140
- Decoquinate?
  - 5x dose suggested (2.5mg/kg)
  - 2 trials indicate limited effect
- Paromomycin?
  - Aminoglycoside?, $60/day

## Treatment /Prophylaxis

- Halofuginone?
  - 3 European studies indicating some effectiveness
  - Canadian study:
    - No difference in daily gain or intakes
    - Did delay shedding and decrease amount shed
  - Not currently available in North America (except emergency approval)
  - Estimated at $10 – 15/ treated calf

J. Dairy Sci. 92:1643–1648
doi:10.3168/jds.2008-1474


**Effect of nitazoxanide on cryptosporidiosis in experimentally infected neonatal dairy calves**

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‡Department of Microbiology and Immunology, C5-181 VMC, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853

## Objective of our study…

…to perform a randomized, blinded, controlled study evaluating the effect of **nitazoxanide (NTZ)** on cryptosporidiosis in experimentally challenged neonatal dairy calves.

## Materials & Methods

- Clean delivery
- Rapid transport to isolation facility
- 23 Holstein bull calves
- 32 Feeding follow up

## Materials & Methods

- Feeding
  - Non-medicated milk replacer
  - 1.5 lbs dry matter/day
  - Twice daily
- Cleaning
  - New bedding daily
  - Separate equipment
  - High pressure, hot water between calves

## Materials & Methods

- Challenge Model
  - 1 x $10^6$ *C. parvum* oocysts
  - 1 hr after feeding #3
  - Serum protein $\geq$ 5 mg/dl
- Outcomes measured:
  - Body weight
  - Health score
  - Fecal score
  - Oocyst count

## Materials & Methods

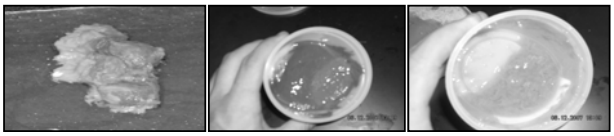
Health Scoring

1) Normal
2) Depressed
3) Very depressed
4) Moribund or dead

## Materials & Methods

Fecal Scoring

1) Normal
2) Mild diarrhea
3) Severe diarrhea

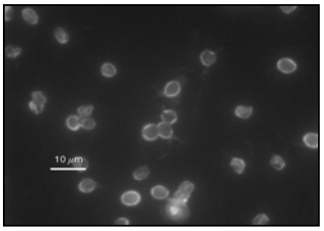


## Materials & Methods

- Treatment Criteria
  - Feeding $\geq$ #11
  - Fecal score $\geq$ 2
- Dose
  - 1.5 g NTZ PO BID x 5 days
  - Equivalent to 4.7 g commercial NTZ paste

## Materials & Methods

- Oocyst counting
  - IFA
- Data analysis
  - Wilcoxan Rank Sum
  - Survival Analysis
  - Chi Square Analysis




http://commons.wikimedia.org/wiki/Image:Cryptosporidium_parvum_01.jpg

## Results

- 13 NTZ treated calves
- 7 placebo treated calves
- Diarrhea
- Palatable
- Easily administered
- Non-toxic

| | Treatment (median) | Control (median) | p-value |
|---|---|---|---|
| Total Protein at feeding 3 | 5.6g/dl | 5.65g/dl | 0.93 |
| Body Weight at feeding 3 | 107 lbs | 103 lbs | 0.8 |
| Onset Oocyst Shedding | 7days | 7days | 0.68 |

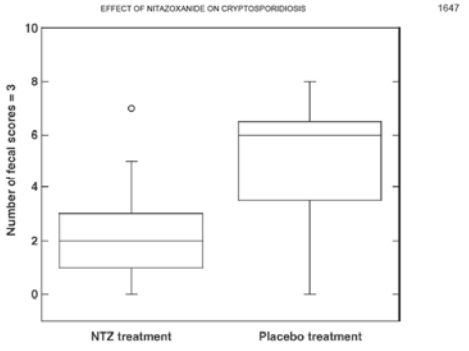



Figure 2. Box and whisker plot of number of feedings with fecal score (FS) equal to 3 (i.e., watery diarrhea). After initiation of treatment with nitazoxanide (NTZ), the median number of feedings with FS = 3 was 2 for the NTZ-treated calves and 6 for placebo-treated calves ($P = 0.06$).

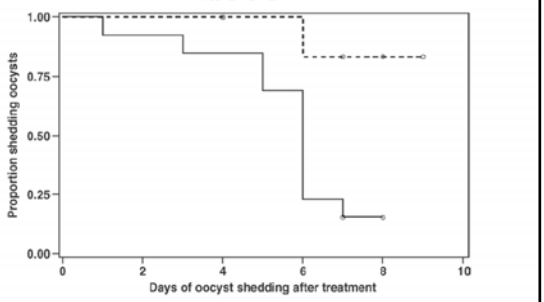



Figure 1. Kaplan-Meier survival curves for time (d) to cessation of oocyst shedding from initiation of treatment in placebo-treated calves (dashed line) and calves treated with nitazoxanide (NTZ; solid line). Fifteen percent of the NTZ-treated calves failed to stop shedding, whereas 85% of the placebo-treated calves were shedding oocysts by the end of the observation period ($P = 0.01$).

## Immune System Management

Cow/Calf

Pathogen ⟷ Environment

(e.g.Salmonella)

(e.g. fecal contamination)

## The Effect of Nutritional Plane on Health and Performance of Dairy Calves After Experimental Infection with *C. parvum*

TL Ollivett, DV Nydam, TC Linden, DD Bowman, M. Van Amburgh

Cornell University
College of Veterinary Medicine

## Objective of our study…

to evaluate the effect of nutritional plane on health and performance of dairy calves after experimental infection with *C. parvum*.

## Materials & Methods – Acquisition

- Clean delivery
- Immediate isolation
- 29 Holstein bull calves
- 42 Feeding (21d) follow up

## Feeding Strategies

- Calves randomized at birth
- Conventional (CN) *v.* High Plane of Nutrition (HPN)
- Commercially available milk replacers
- Feeding rates based on metabolic body weight (MBW) (body mass that significantly contributes to metabolism)
  - MBW = $(kg)^{0.7}$

## Current Feeding Standards

- "female calves in the US destined for herd replacements should be fed restricted amounts of milk or milk replacer (typically 8-10% of birth weight) to encourage early consumption of calf starter"
- "growth rates… and feed efficiency is lower than that in the young of other farm animals allowed to consume milk ad libitum"

  - NRC, 2001

## Amount of MR/Milk DM to meet Maintenance Requirements and Gain 1lb/day

Body weight, lbs

Temperature

| | 68 | 50 | 32 | 15 | 5 | -5 |
|---|---|---|---|---|---|---|
| 60 | 1.1 | 1.2 | 1.4 | 1.5 | 1.6 | 1.7 |
| 80 | 1.2 | 1.4 | 1.6 | 1.7 | 1.9 | 2.0 |
| 100 | 1.4 | 1.6 | 1.8 | 2.0 | 2.2 | 2.5 |
| 120 | 1.6 | 1.8 | 2.1 | 2.2 | 2.6 | 2.8 |

## Environment Effects Maintenance Requirements

- Thermoneutral zone for calves <21d is 59 – 80 F
- In New York, ~160 d below 59 F
- For calves >21 days the lower critical temp = 42 F

## Feeding Calculations

CN for *days 1-21*

| Calf ID | BW, KG | MBW | Feeding rate | Mcal/d | MR Mcal/kg | MR, kg/d | MR, lb/d |
|---|---|---|---|---|---|---|---|
| 1 | 50 | 18.80 | 0.130 | 2.444 | 4.940 | 0.495 | 1.089 |

HPN for *days 1-7*

| Calf ID | BW, KG | MBW | Feeding rate | Mcal/d | MR Mcal/kg | MR, kg/d | MR, lb |
|---|---|---|---|---|---|---|---|
| 2 | 50 | 18.80 | 0.230 | 4.325 | 5.060 | 0.855 | 1.880 |

HPN for *days 8-21*

| Calf ID | BW, KG | MBW | Feeding rate | Mcal/d | MR Mcal/kg | MR, kg/d | MR, lb/d |
|---|---|---|---|---|---|---|---|
| 2 | 50 | 18.80 | 0.300 | 5.641 | 5.060 | 1.115 | 2.453 |

## Feeding Summary

**CN**

- 20% protein 20% fat
- 1 lb dry matter (DM) per day
- 2.4 Mcals/day

**HPN**

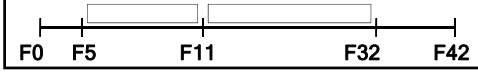
- 28% protein 20% fat
- 2.5 lbs DM per day
- 5.6 Mcals/day

Maintenance requirement = 1.75 Mcal/day

(thermoneutral zone; no pathogen load)

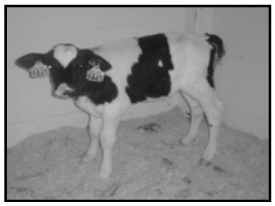
## Materials & Methods - Infection

- Serum protein ≥ 5 g/dl
- 1 x $10^6$ *C. parvum* oocysts
- 1 hr after feeding 5



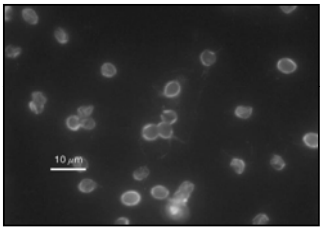
## Materials & Methods- Outcomes

- Health score
- Fecal score
- Oocyst count
- Packed Cell Volume
- Dry matter intake (DMI)
- Average daily weight gain (ADG)
- Feed Efficiency



## Materials & Methods – Analysis

- Oocyst counting
  - IFA
- Data analysis
  - Wilcoxon Rank Sum
  - Regression Analysis
  - Chi-Square
  - Survival Analysis




http://commons.wikimedia.org/wiki/Image:Cryptosporidium_parvum_01.jpg

## Results

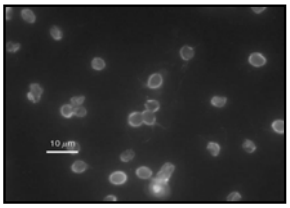
- 11 HPN calves
- 9 CN calves
- 100% Diarrhea
- 0 Treatments

| | HPN (median) | CN (median) | p-value |
|---|---|---|---|
| Total Protein at feeding 5 | 5.5g/dl | 5.3g/dl | 0.4 |
| Body Weight at feeding 5 | 103 lbs | 104 lbs | 0.8 |
| Packed Cell Volume at feeding 5 | 30% | 32% | 0.15 |

## Results

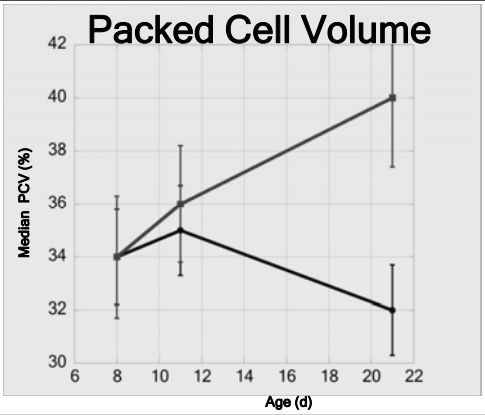
No Difference
(P>0.7)

- Peak shedding
- Total shedding
- Onset of shedding
- Duration of shedding




http://commons.wikimedia.org/wiki/Image:Cryptosporidium_parvum_01.jpg

## Packed Cell Volume




CN
HPN

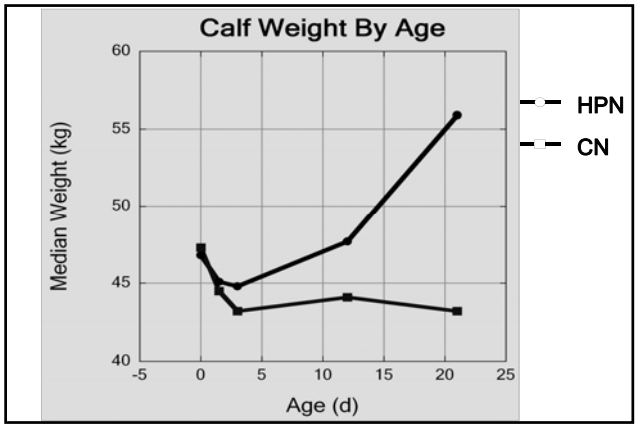
D8: HPN vs CN
P=0.3

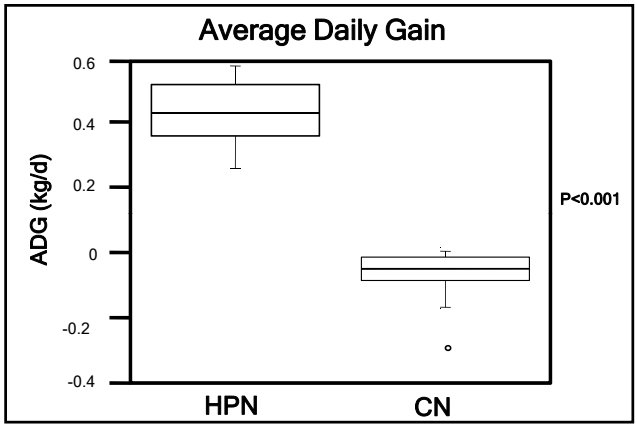
D8 HPN vs
D21 HPN
P=0.5

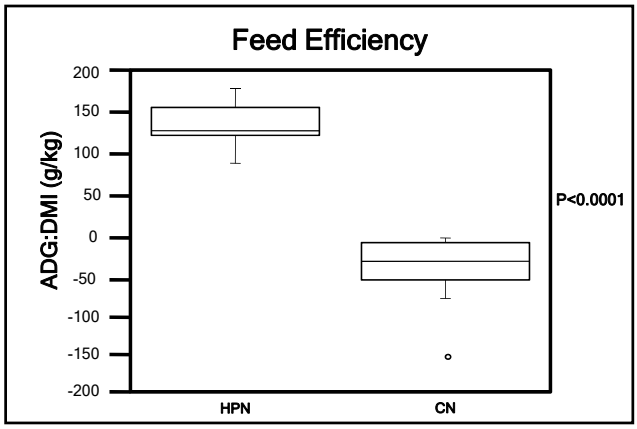
D8 CN vs
D21 CN
P=0.04

## Resolution of diarrhea

- Regression Analysis
  - HPN slope = - 0.1
  - CN slope = -0.01
  - P = 0.03
- Interpretation
  - FS improve 10x per day

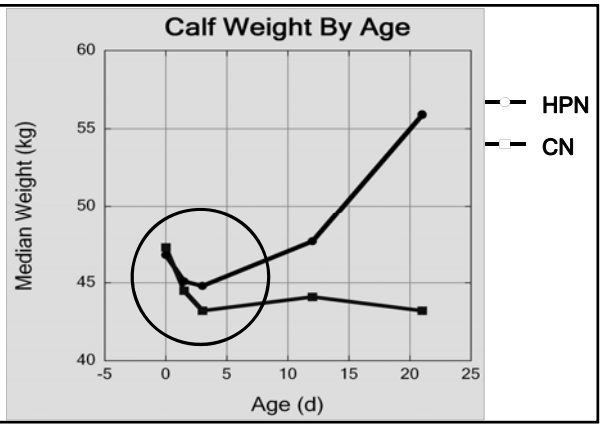

Calf Weight By Age
Median Weight (kg)
60
55
50
45
40
-5
0
5
10
15
20
25
Age (d)
HPN
CN


Average Daily Gain
ADG (kg/d)
0.6
0.4
0.2
0
-0.2
-0.4
HPN
CN
P<0.001


Feed Efficiency
ADG:DMI (g/kg)
200
150
100
50
0
-50
-100
-150
-200
HPN
CN
P<0.0001

## Conclusions

- HPN reduces the effect of disease due to *C. parvum* in neonatal dairy calves
- Calf behavior should be predominant factor affecting calf feeding; not fecal consistency




## Effect of nutritional plane on health, performance and muscle metabolism in neonatal dairy calves


- Theresa L. Ollivett, DVM
- Daryl Nydam, DVM, PhD; Mike VanAmburgh,PhD;
- Joe Wakshlag, DVM, PhD, DACVN

## Calf Weight By Age


Ollivett et al., 2009. AABP Proceedings

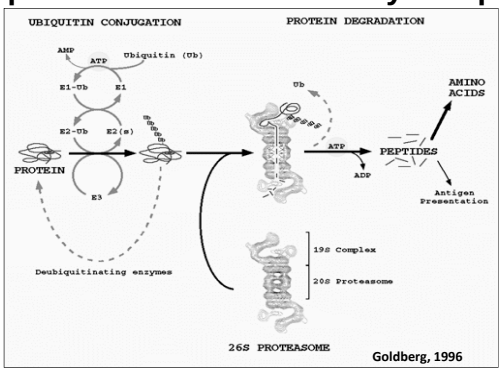
## Questions

- Important?
- Characterize?
- Hydration status?
- Lipolysis?
- Muscle wasting?

## Questions

- Important?
- Characterize?
- Hydration status? — PCV,TP,Creatnine
- Lipolysis? — NEFA
- Muscle wasting? — Markers of muscle metabolism

## Ubiquitin Proteasome Pathway-Atrophy




Goldberg, 1996

## Atrogin – muscle atrophy

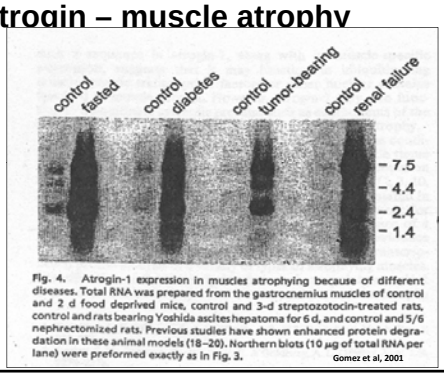



Fig. 4. Atrogin-1 expression in muscles atrophying because of different diseases. Total RNA was prepared from the gastrocnemius muscles of control and 2 d food deprived mice, control and 3-d streptozotocin-treated rats, control and rats bearing Yoshida ascites hepatoma for 6 d, and control and 5/6 nephrectomized rats. Previous studies have shown enhanced protein degradation in these animal models (18–20). Northern blots (10 μg of total RNA per lane) were preformed exactly as in Fig. 3.

Gomez et al, 2001

## Objective

- evaluate the effect of **nutritional plane** on **health, performance** and **muscle metabolism** in neonatal dairy calves

## Materials & Methods – Acquisition

- Clean delivery
- Immediate isolation
- 20 Holstein calves (M & F)
- 28 Feeding (14d) follow up

## Materials & Methods – Treatment

- Treatment Groups
  - Conventional Nutrition (CN)
  - Higher Plane Nutrition (HPN)

Maintenance energy requirement = 1.75 Mcal/day
(thermoneutral zone; no pathogen load)

**CN for days 1-14** **20% Protein 20% Fat**

| ID | BW, kg | MBW (kg) | Feeding rate | Mcal/d | MR, Mcal/kg | MR, lb/d |
|---|---|---|---|---|---|---|
| 1 | 50 | 18.80 | 0.13 | 2.44 | 4.90 | 1.00 |

**HPN for days 1-7** **28% Protein 20% Fat**

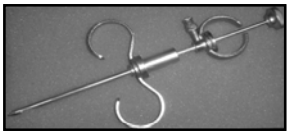
| ID | BW, kg | MBW (kg) | Feeding rate | Mcal/d | MR, Mcal/kg | MR, lb/d |
|---|---|---|---|---|---|---|
| 2 | 50 | 18.80 | 0.23 | 4.33 | 5.06 | 1.88 |

**HPN for days 8-14** **28% Protein 20% Fat**

| ID | BW, kg | MBW (kg) | Feeding rate | Mcal/d | MR, Mcal/kg | MR, lb/d |
|---|---|---|---|---|---|---|
| 2 | 50 | 18.80 | 0.30 | 5.64 | 5.06 | 2.45 |

## Materials & Methods- Outcomes

- Health score
- Fecal score
- Packed Cell Volume
- Serum Total Protein
- NEFA, creatinine
- Body Weight
- Muscle biopsy*



*Am J Vet Res. 1995. 56(8):982-5

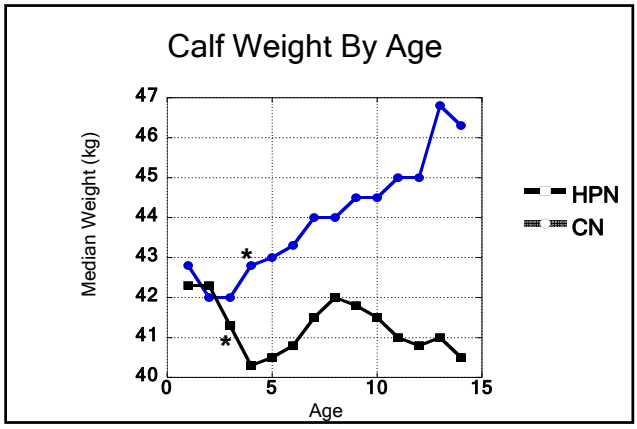
## Materials & Methods – Analysis

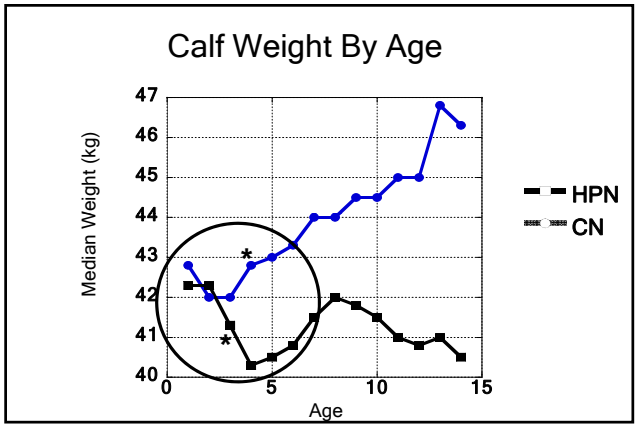
- Atrogin
  - Western blot
  - Densitometry
- Data
  - Wilcoxon Rank Sum
  - Regression Analysis
  - Chi-Square

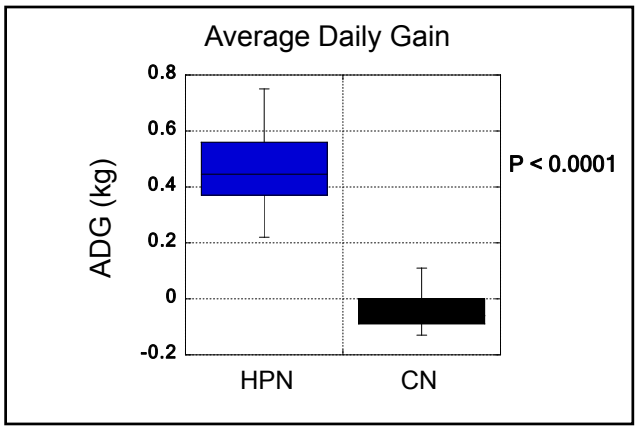
## Results

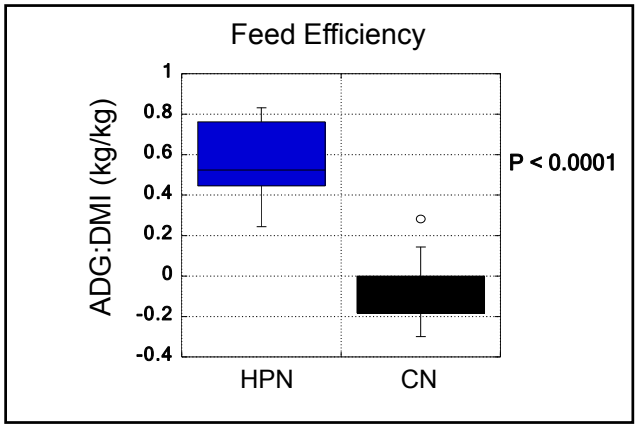
- n=10 HPN
- n=10 CN
- 3 treated
  - dehydration
- 1 died
  - Abomasitis

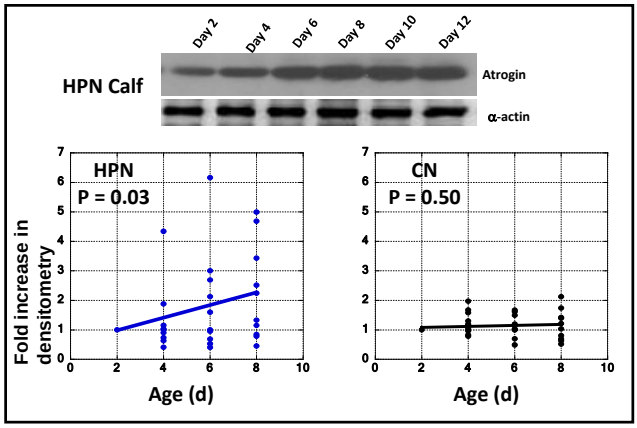
| | HPN (median) | CN (median) | P value |
|---|---|---|---|
| Body Wt | 42.75 kg | 42.25 kg | 1.0 |
| TP day 3 | 5.9 g/dL | 5.7 g/dL | 0.40 |
| TP day 14 | 5.6 g/dL | 5.6 g/dL | 0.88 |
| PCV day 1 | 36% | 35% | 0.88 |
| PCV day 14 | 32% | 28% | 0.07 |
| NEFA day 1 | 0.095 | 0.29 | 0.05 |
| NEFA day 7 | 0.25 | 0.27 | 0.20 |
| Creat day 1 | 2.5 | 2.5 | 0.50 |


Calf Weight By Age
Median Weight (kg)
47
46
45
44
43
42
41
40
0
5
10
15
Age
HPN
CN
*
*


Calf Weight By Age
Median Weight (kg)
47
46
45
44
43
42
41
40
0
5
10
15
Age
HPN
CN
*
*


Average Daily Gain
ADG (kg)
0.8
0.6
0.4
0.2
0
-0.2
HPN
CN
P < 0.0001




## Conclusions

- Upregulation of proteolytic pathway (atrogin) occurs in well fed neonatal calves
  - Likely to due muscle turnover during growth
- Early weight loss is preventable
  - Not solely related to hydration status, fat mobilization, or muscle wasting

## Acknowledgements


- Tom Earleywine, PhD
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- FAME 2009
  - Josh Boyden, Blake Nguyen, Molly Hurley, Karen James, Matt Chuff, Steve Furst, Desiree Gentile, Lindsay Goodale


## Questions?